

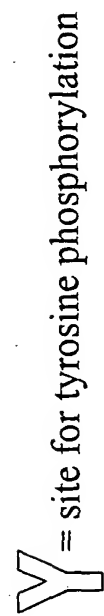
[illegible]

FIG. 1

Enhanced inhibition of NFAT by PAG with mutation of its PDZ-binding motif

FIG. 2 A.

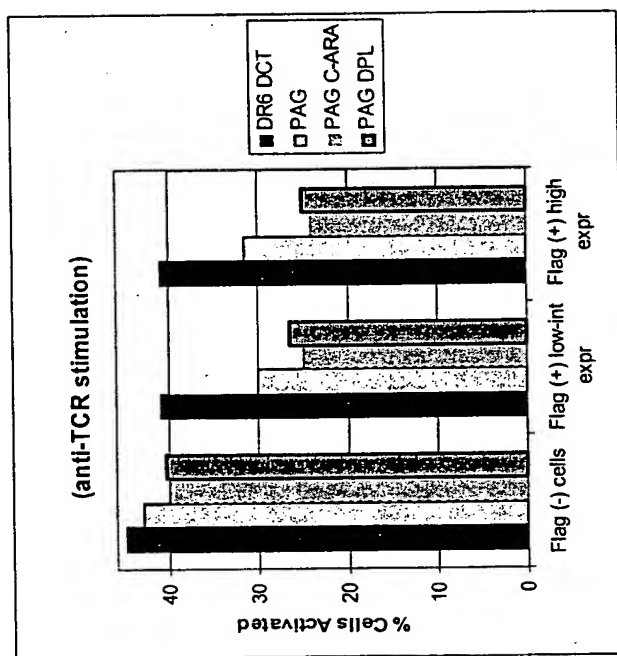
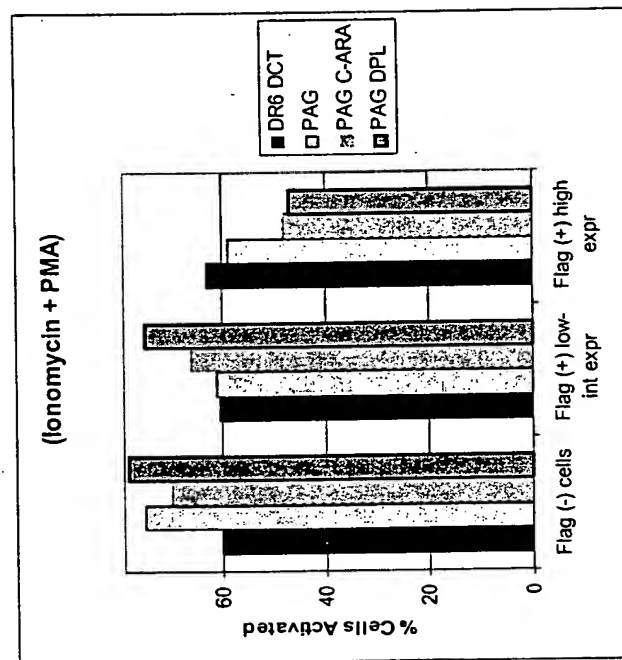


FIG. 2 B.





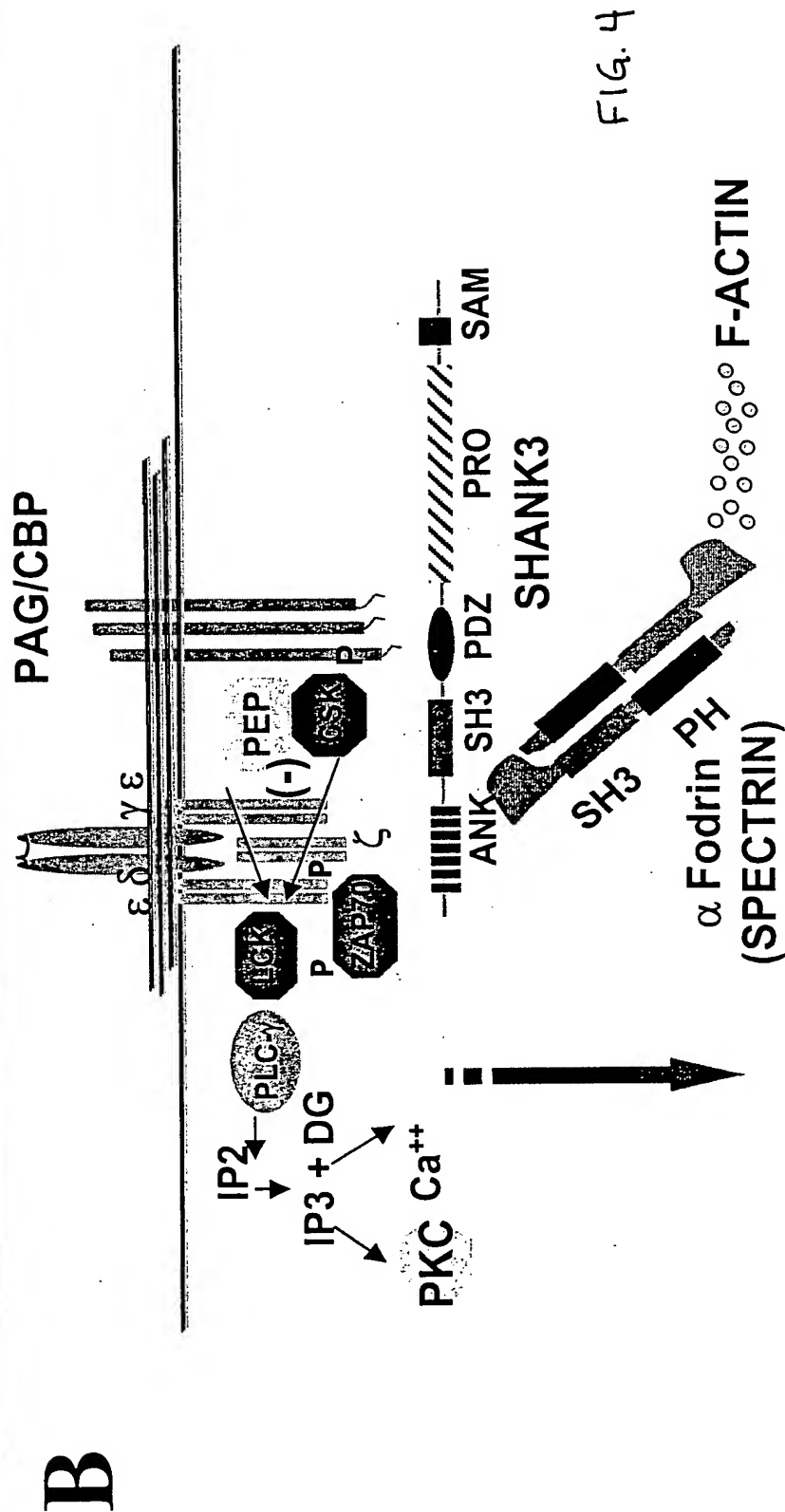
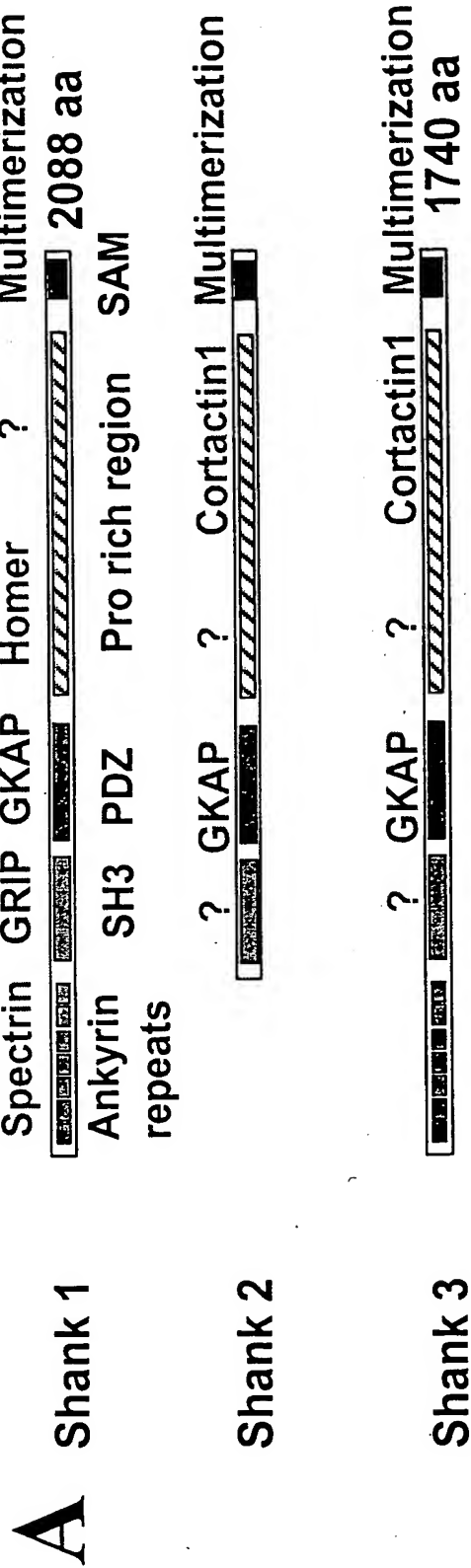


FIG. 4

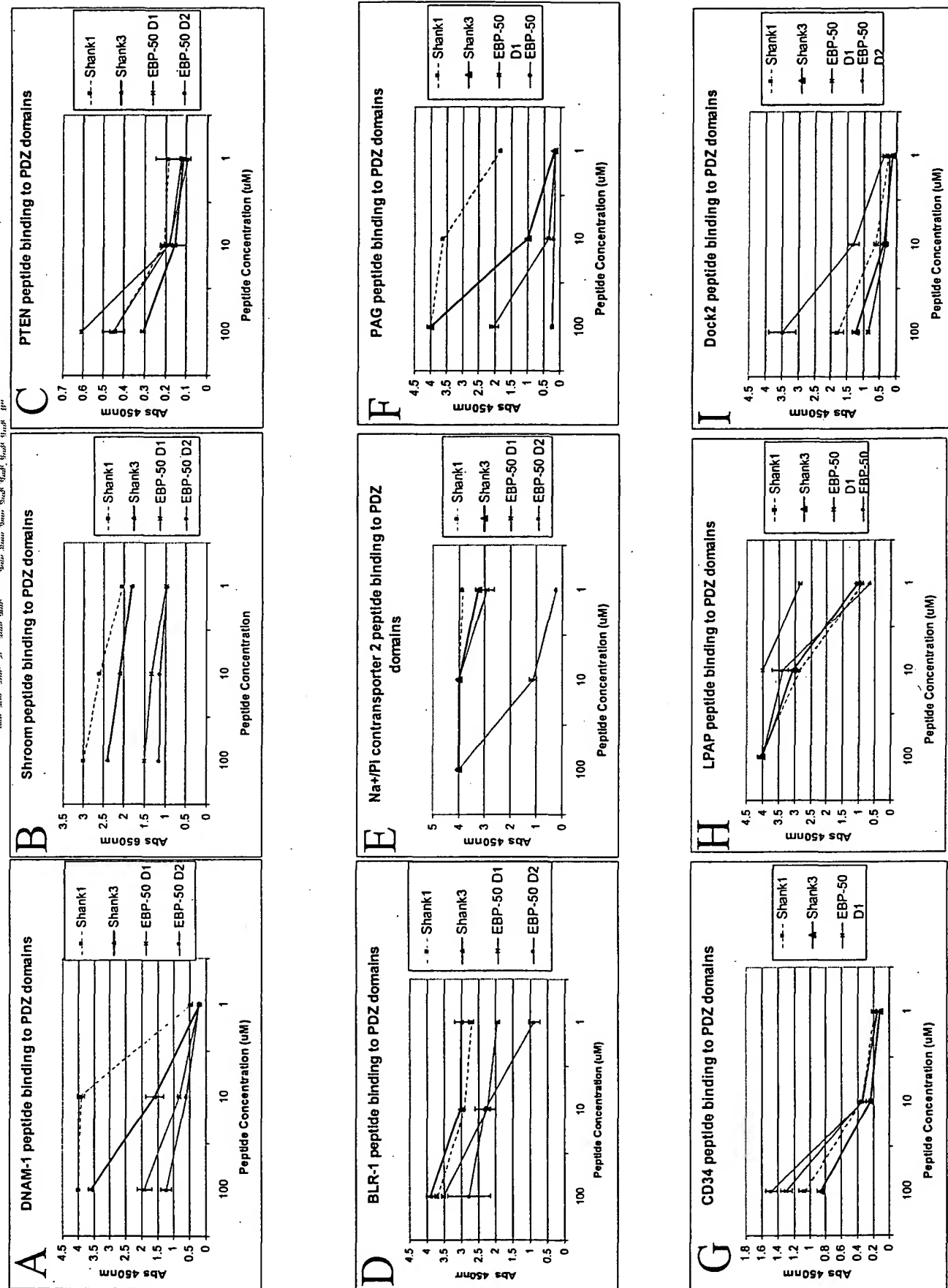


Figure 5

[illegible]

## +OKT3

# CMD CMD

**LAT**

**Lck**

**PKCθ**

# LFA-1

# WASP

CSK

# GRIP

# hDig-1

# CASK

## Dvl-2

# GADS

# IQGAP

# PROTEINS CONTAINING PDZ DOMAINS

## EXPRESSION IN T CELLS

hDIg/SAP97

PSD95 1 PDZ PDZ PDZ SH3 GK 723

Chapsyn  
1 H-PDZ-PDZ-PDZ-SH3-GK-H  
870

[illegible]

**CASK** 1 [CaM-binding domain] — PDZ — SH3 — TSGK — 961

Shank 1 ANK SH3 PDZ PRO PRO 1863

Dv1 1 PDZ 691

1 736

Pick1 1 PDZ-CC 416

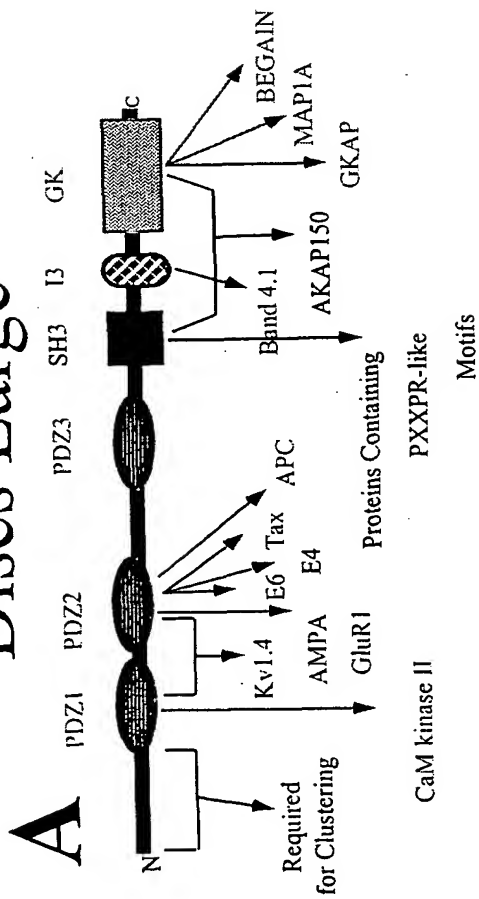
1 CNK SAM CRIC PDZ PRO PRP 729

PDZ rho GEF

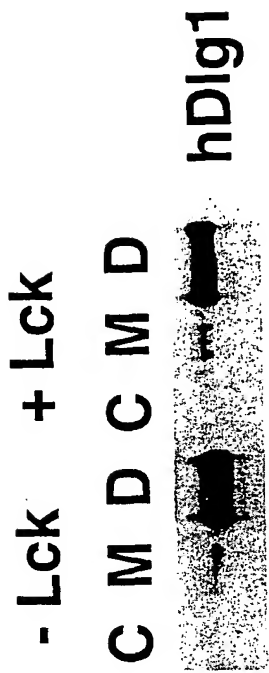
1 PDZ PRO PH 1522 +/-

Fig. 6

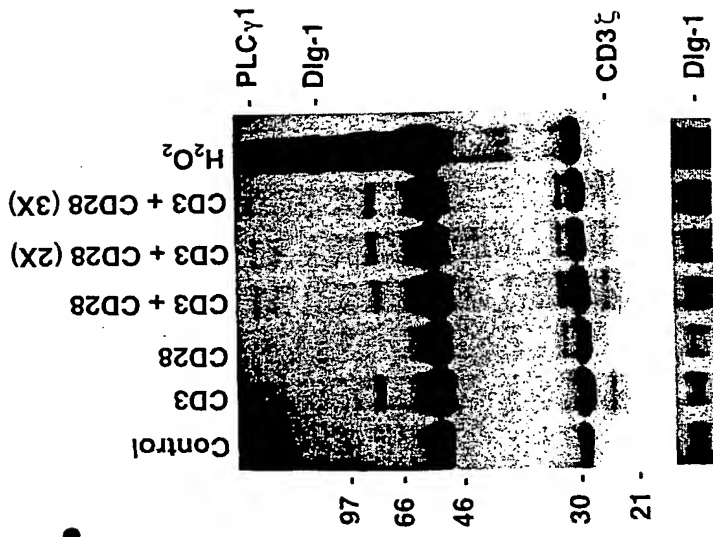
# Discs Large



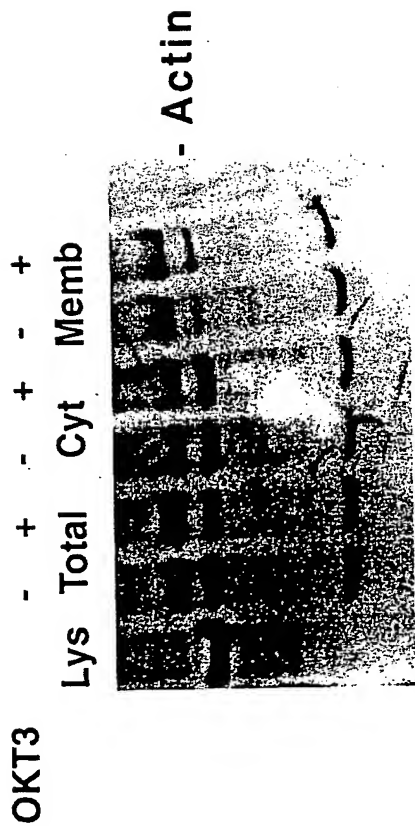
**B.**



**D.**



**C.**



hDlg-1 ip / Actin blot

FIG. 7

100 kDa

NGK PDZ1-3 NPDZ1-3 SH3IGK hDlg1 ΔPDZ1-3

Bound  
Cbl

hDlg  
fusions

Total  
Cbl

Multiple  
Domains of  
Dlg are  
Required for  
Interaction  
with Cbl

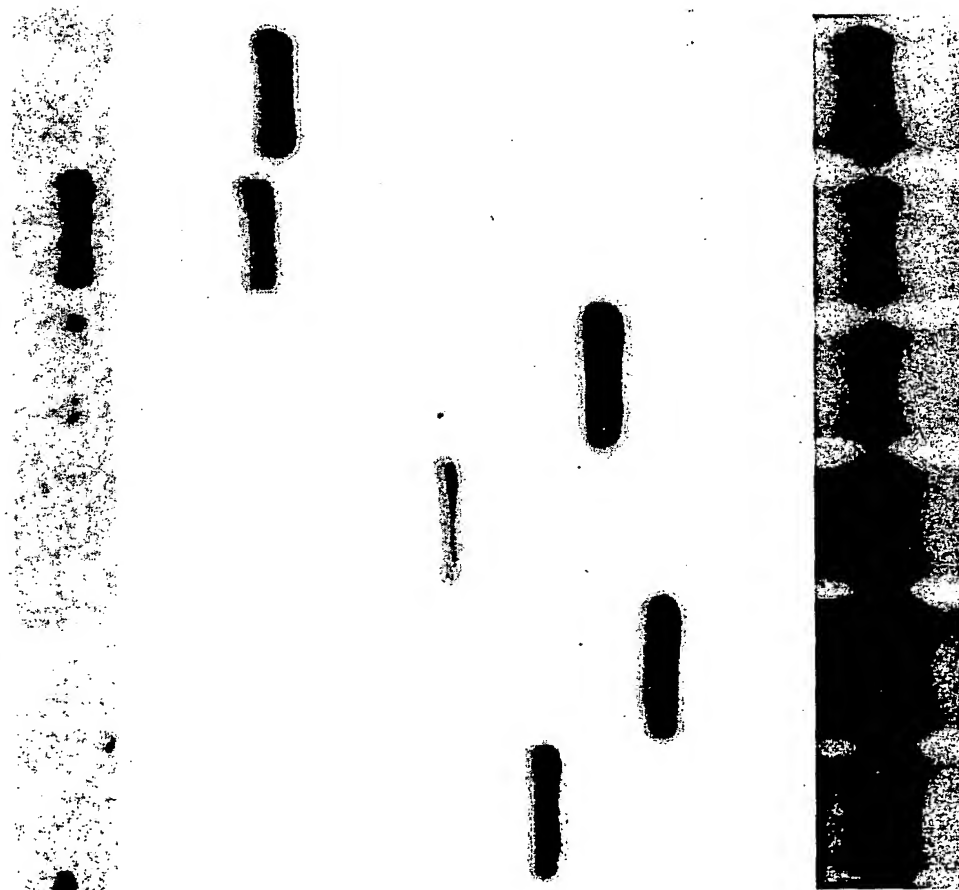
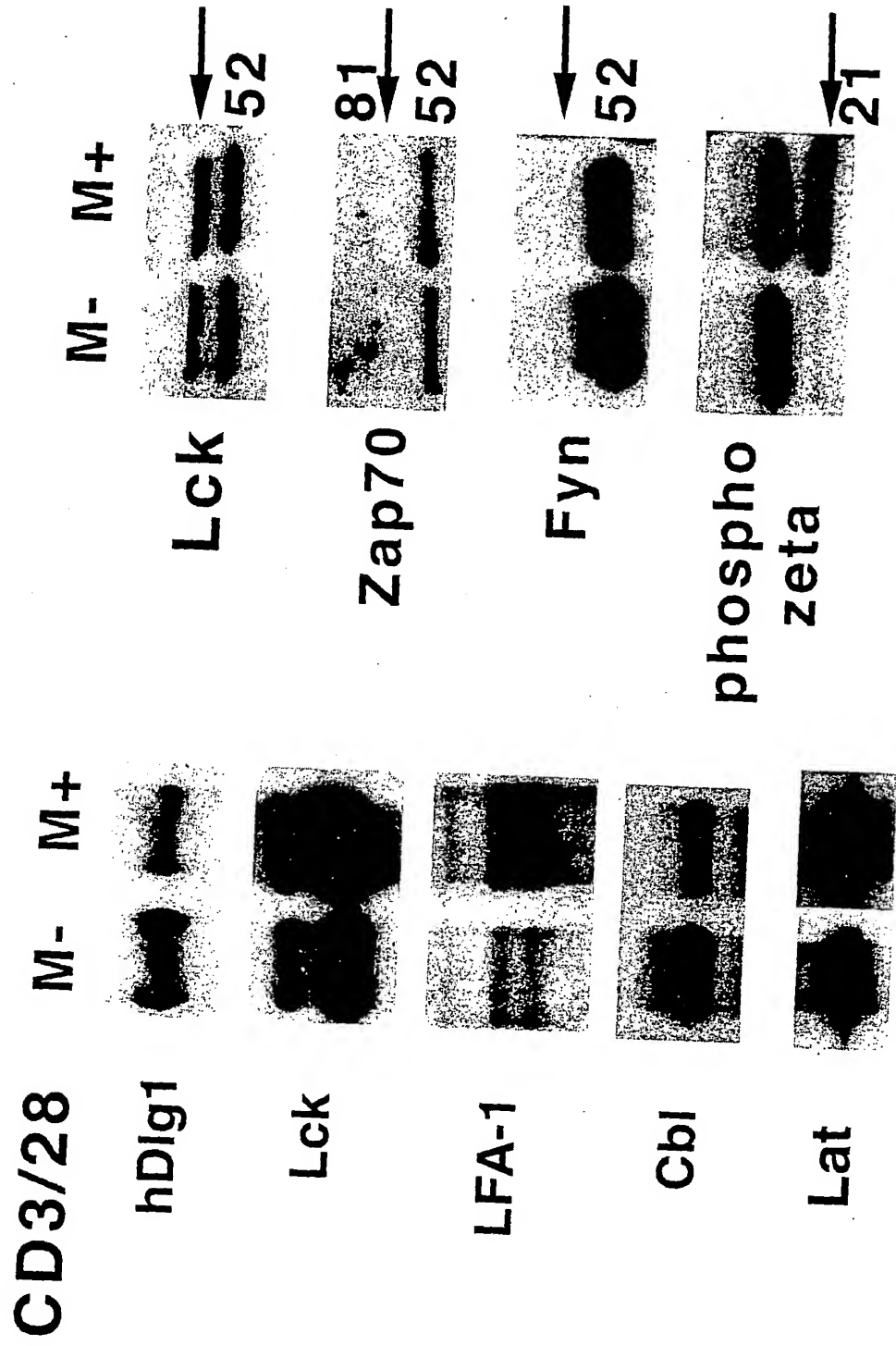


FIG. 8



20050303: 12000000

# Many Important Signaling and Adhesion Molecules Bind Dlg in T cells



Ip: Dlg; Blot: Abs Indicated

FIG. 9

# Discs Large Interaction Partners

Discs Large











	Lck	Fyn	Zap70	CD3 $\zeta$	LAT	SLP76	Cbl	Vav	cdc42
Dlg	+	-	-	+	+	-	+	-	-

	14-3-3	GADS	Tpl2	CaMKII	LFA-1	$\beta$ 3 int	VLA2- $\alpha$	CASK
Dlg	-	-	-	+	+	-	-	+

FIG. 10

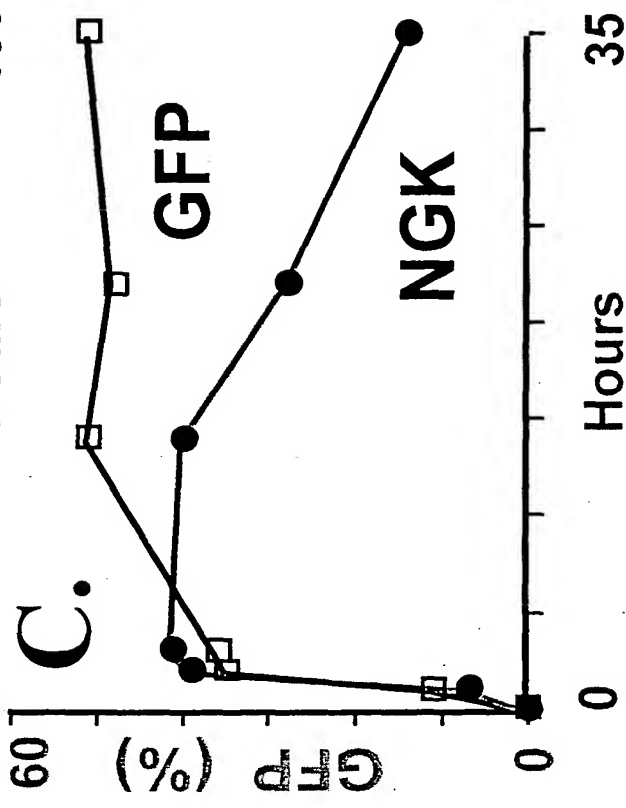
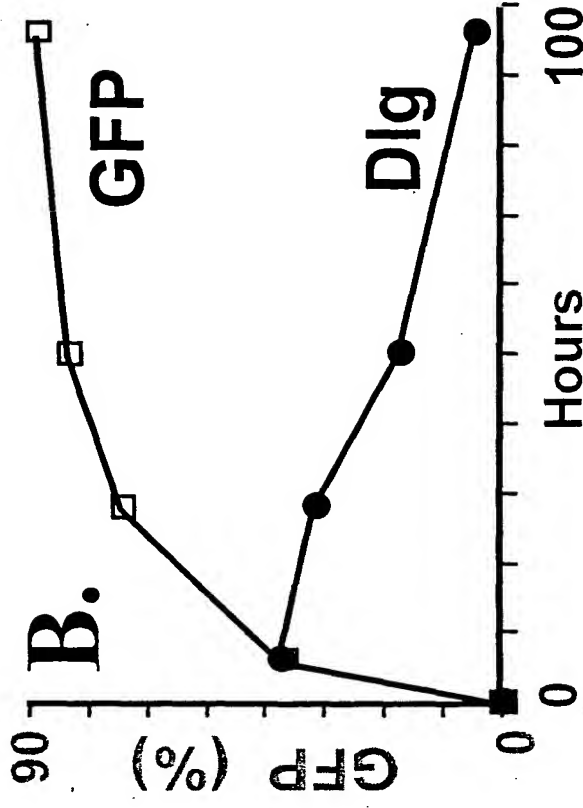
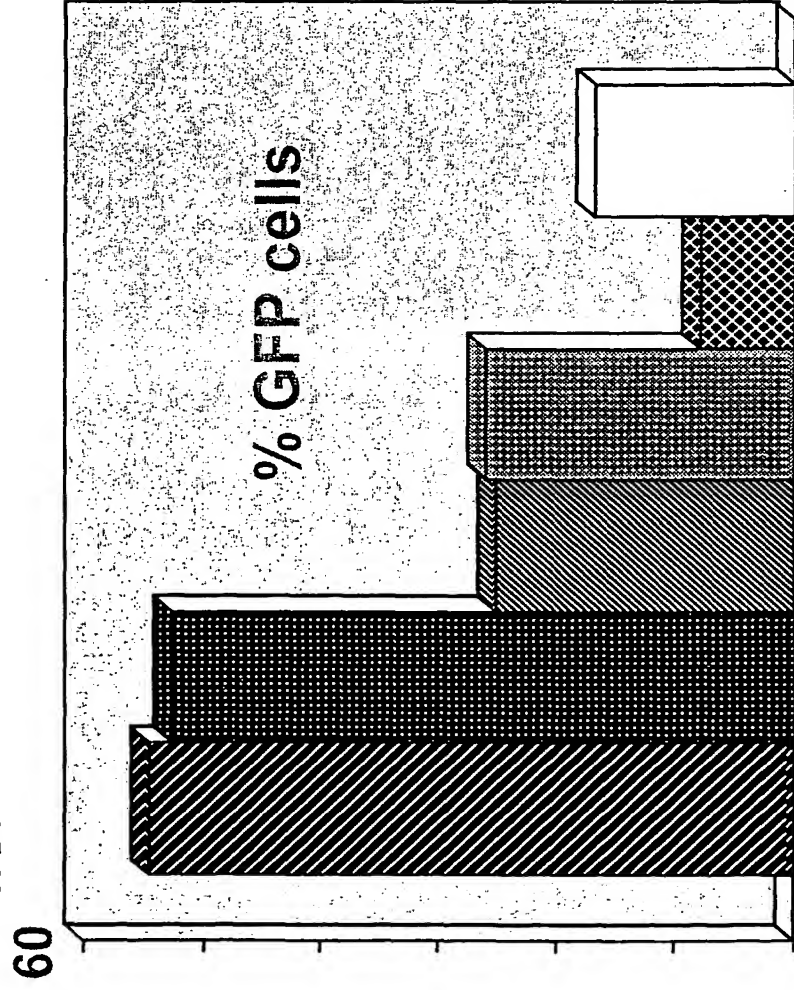
# Gross Mapping of Interactions

Lck CD3 LAT Cbl

<b>Dlg</b>		+	+	+	++
<b>GFP</b>		-	-	-	-
<b>NGK</b>		+	+	-	-
<b>GK</b>		-	-	-	-
<b>Dlg(1-218)</b>		+	+	+/-	
<b>NPDZ1-3</b>		+			-
<b>PDZ1-3</b>		-	-	-	-
<b>SH3I3GK</b>		-			+

# Discs Large Induces Cell Death

**A**



# Anatomy of the Death Response

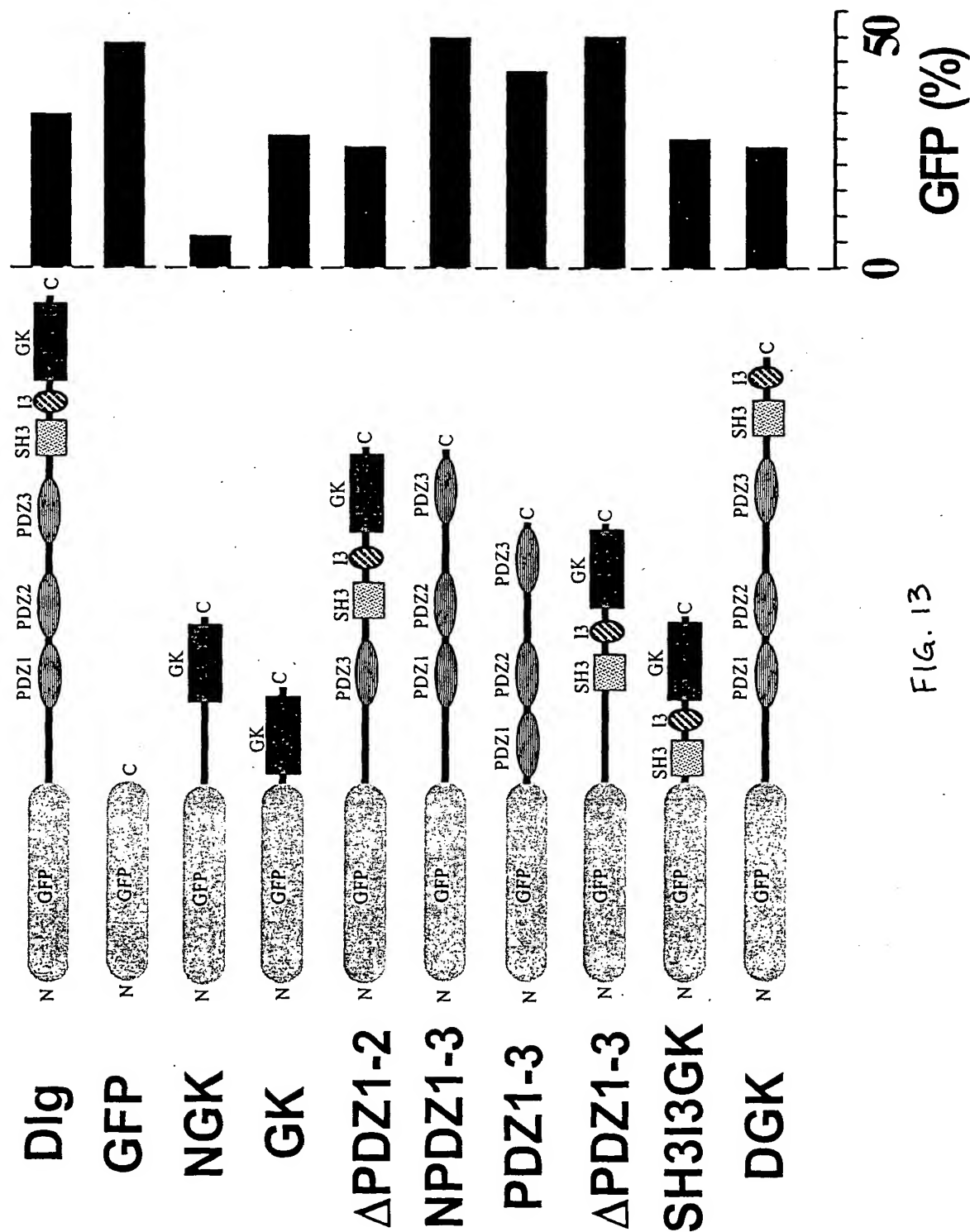
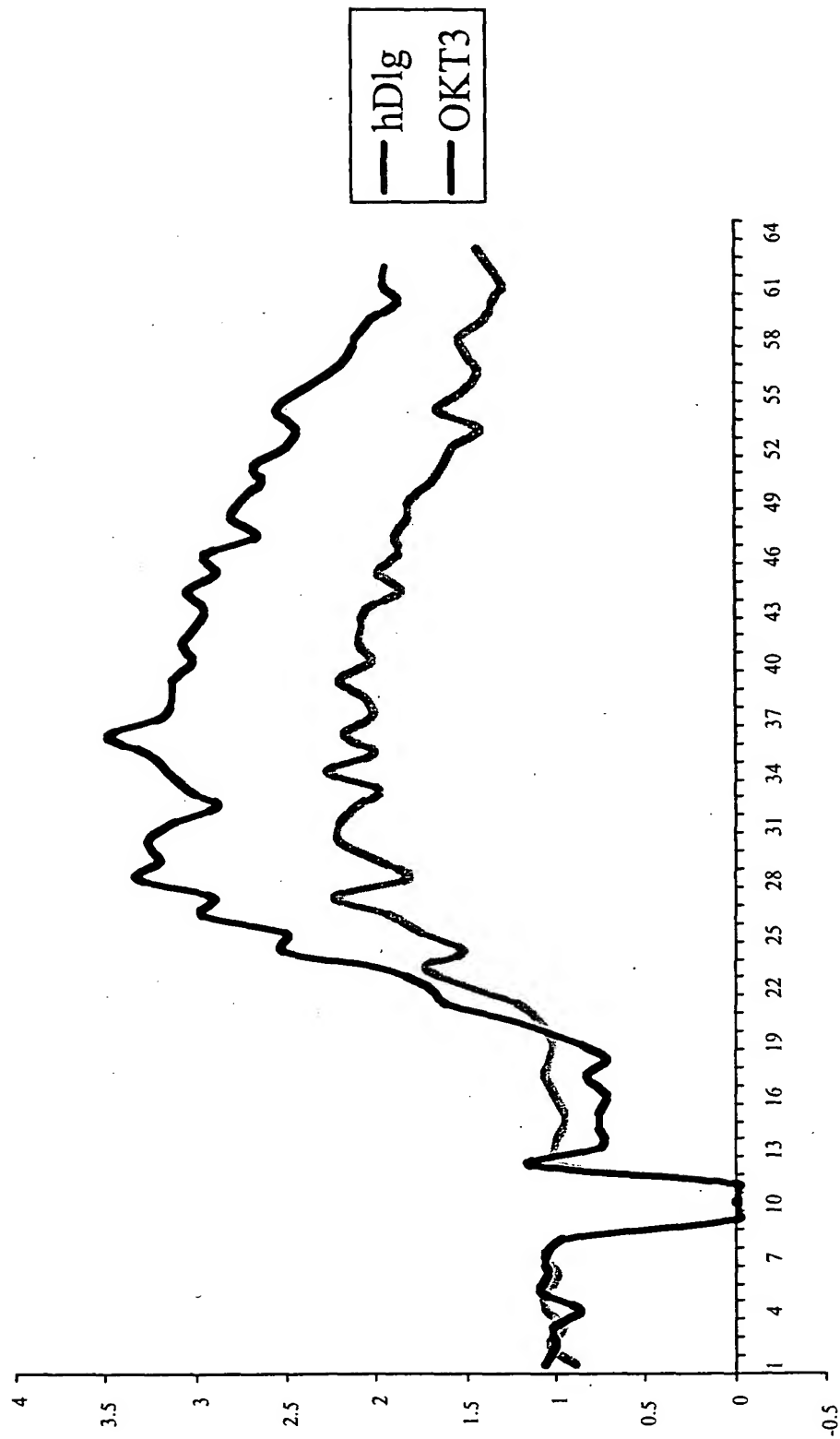


Fig. 13

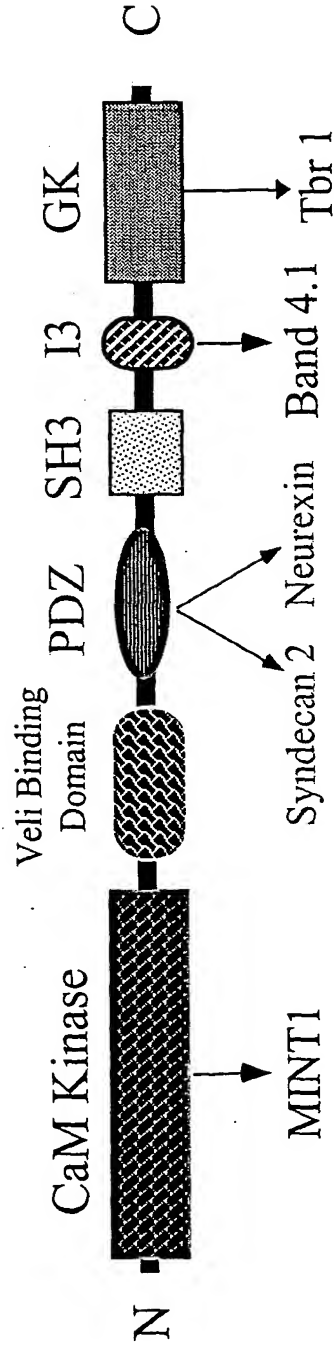
## hDlg Attenuates $\text{Ca}^{++}$ Mobilization



Time in Seconds / 8

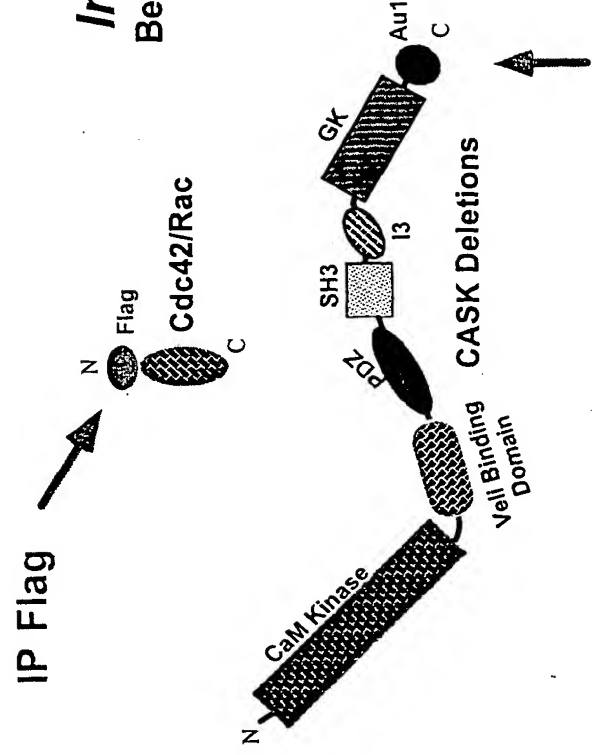
FIG. 14

# A CASK Domain Structure



B

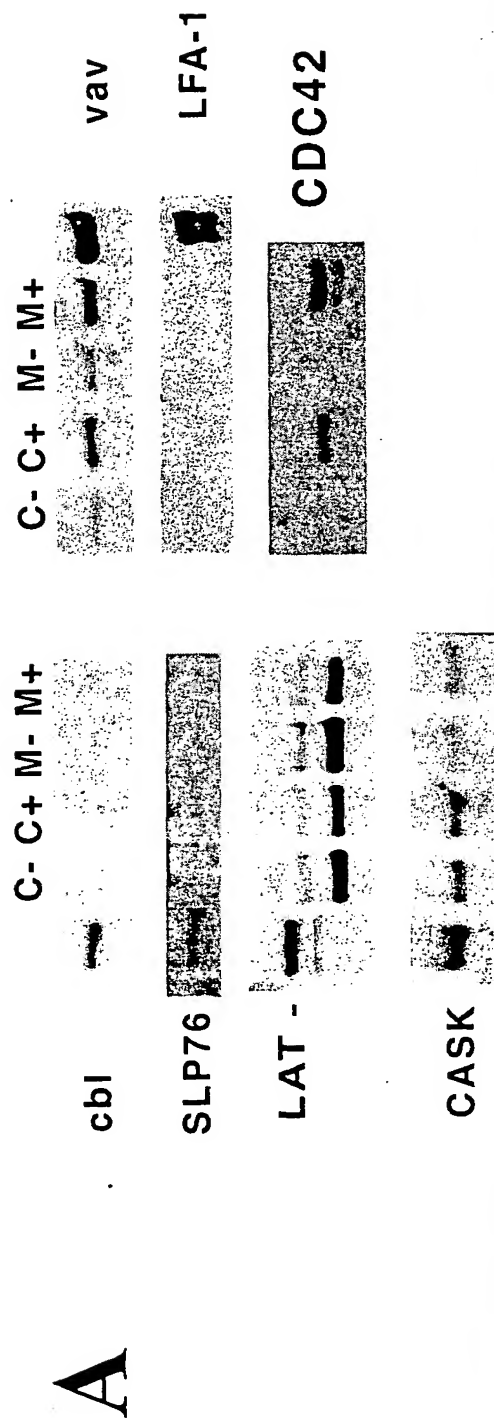
## In vivo Association Studies Between Cdc42/Rac and CASK Deletions



Blot for Au1

FIG. 15

# CASK interactions in Jurkat cells



# CASK interactions in 293T cells

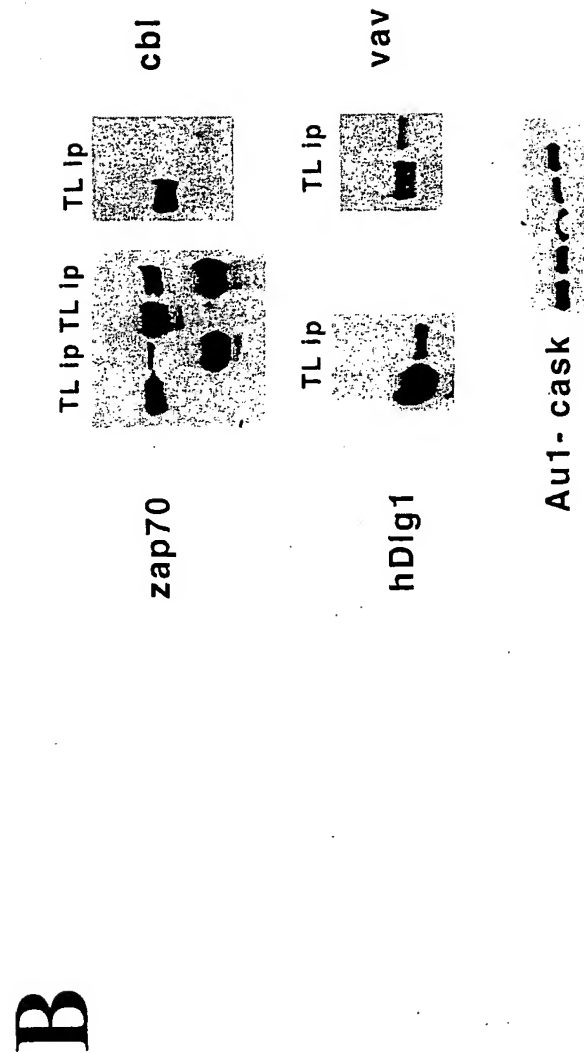


FIG. 16



# Activation-Dependent Association of Signaling Molecules with CASK

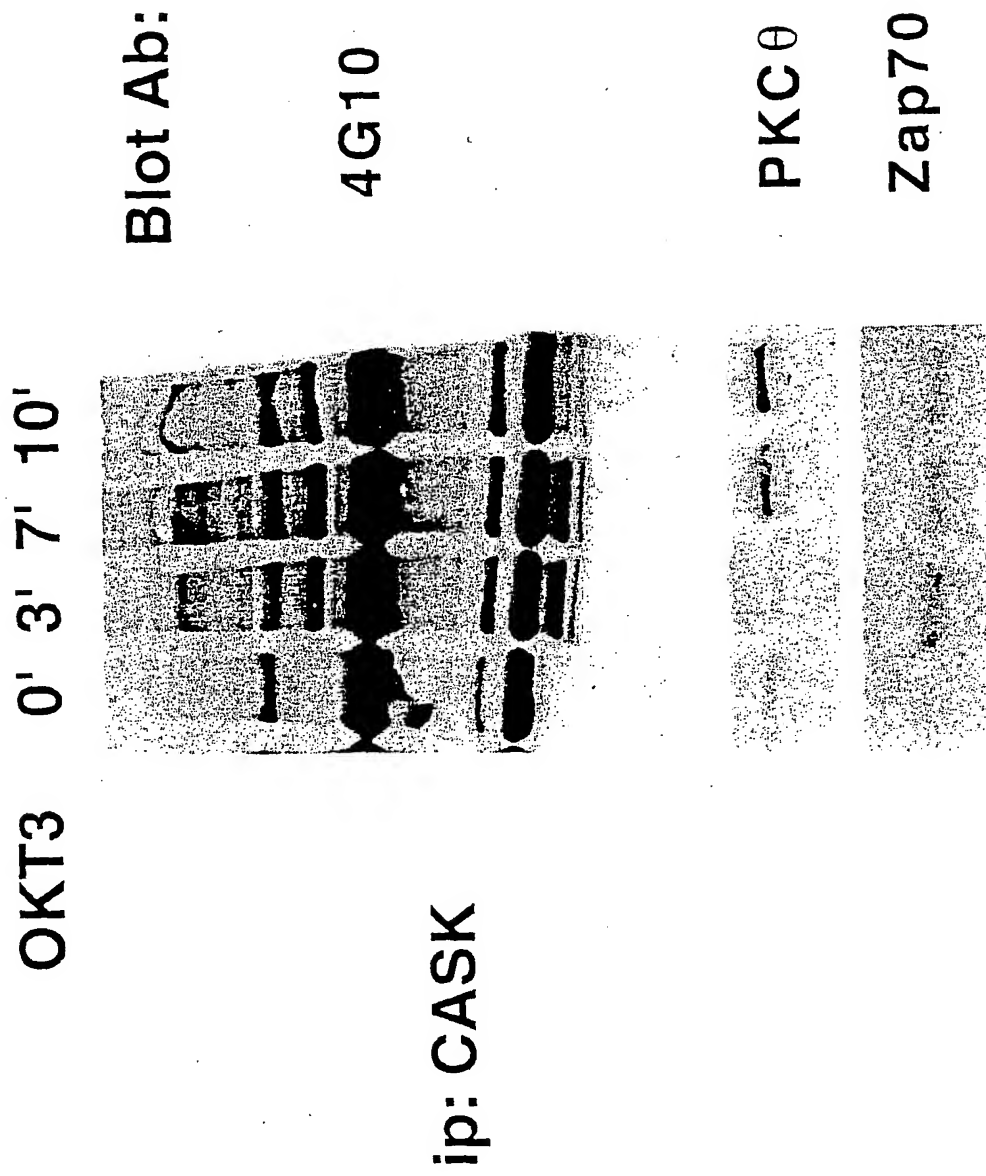


FIG. 17

# IP: Cdc42/Rac

## Blot: CASK Deletions

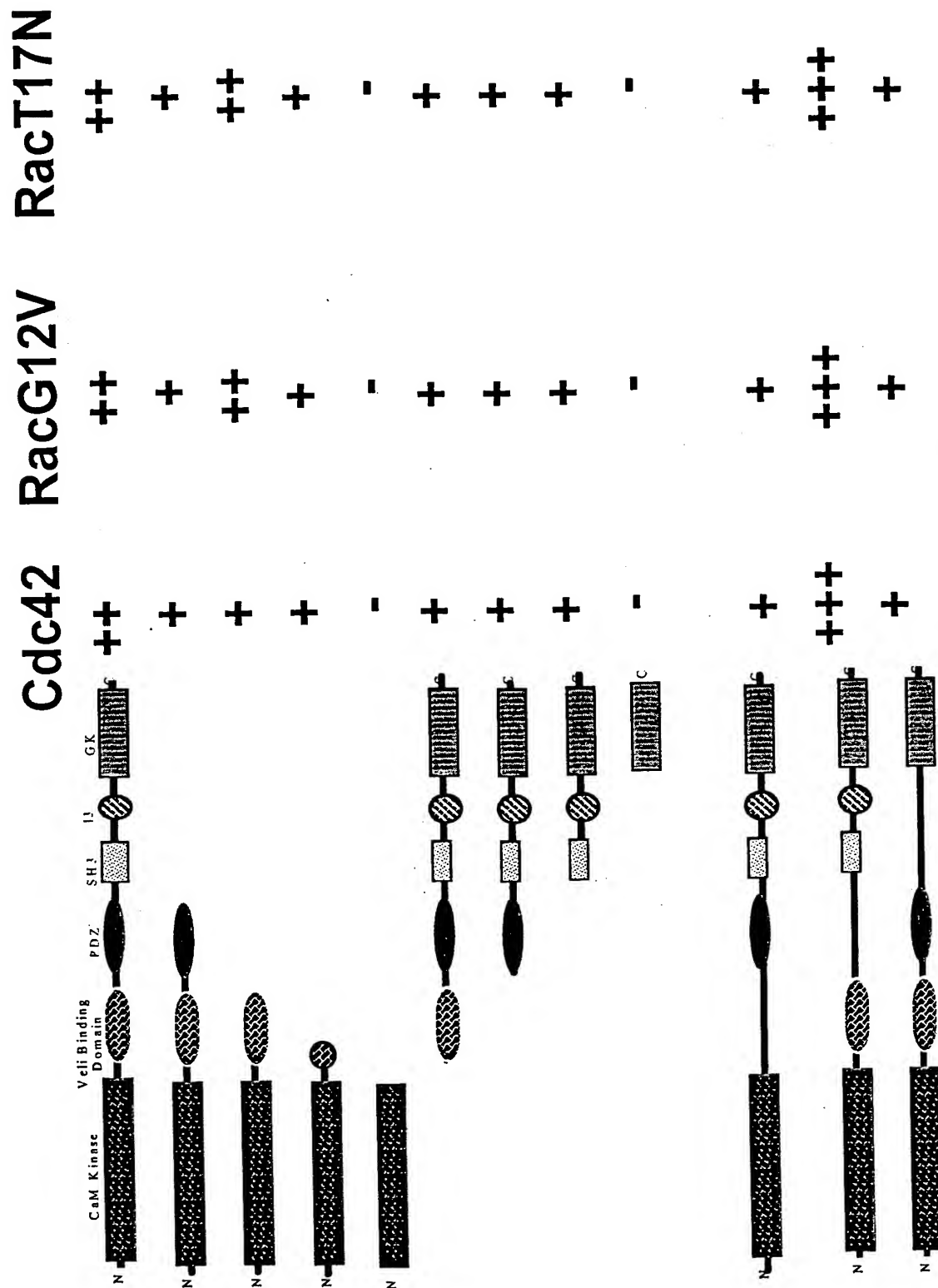


FIG. 18

2005-03-23 14:00:00

## IP: Cdc42

### Blot: CASK Deletions

	1-909	1-600	1-509	1-337	1-909	321-909	481-909	581-909	691-909	DD2	DD3	DD4
--	-------	-------	-------	-------	-------	---------	---------	---------	---------	-----	-----	-----

Blot:  
CASK

Expression  
Control:

CASK

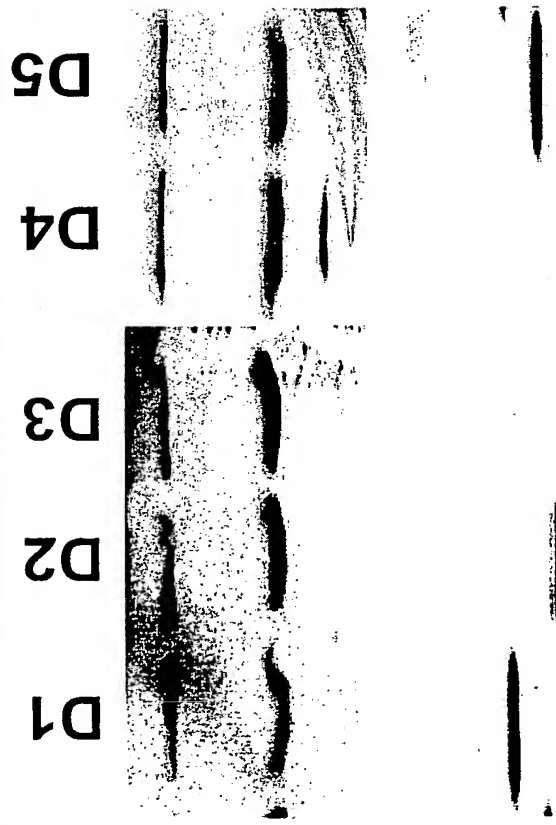
Cdc42

# **Cdc42 RacG12V RacT17N**



**A**

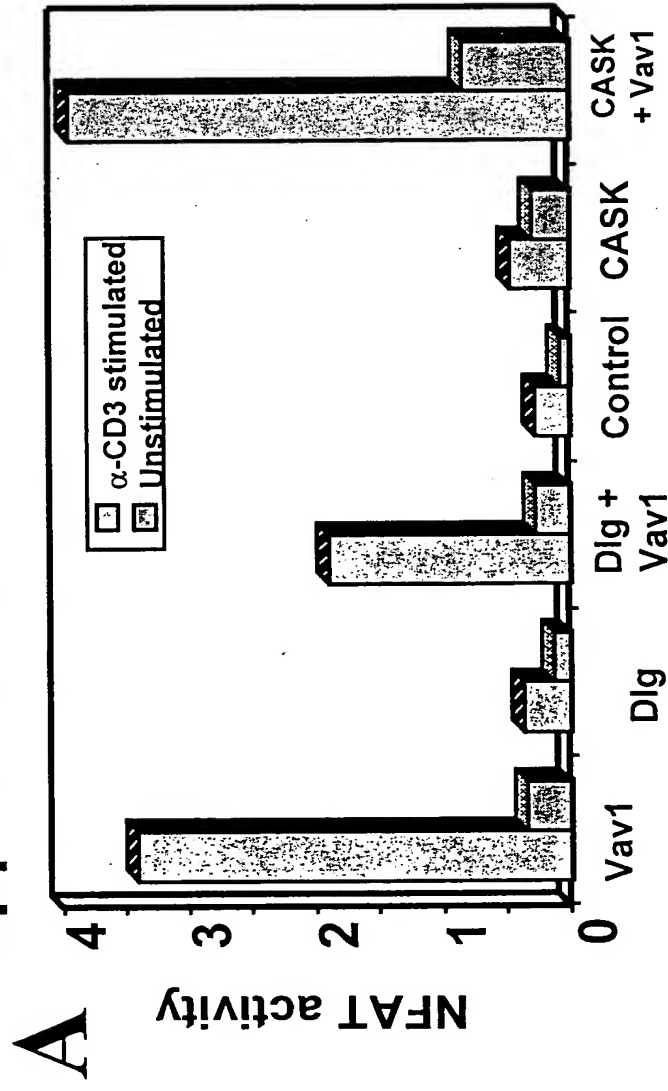
-	-	-	-
-	-	-	-
-	-	-	-
+	+	+	+
-	-	-	-



**B**

IP: RacG12V  
Blot: CASK Domains

# Opposite Actions of CASK and Dlg on NFAT



NF-κB Induction  
in Jurkat Cells

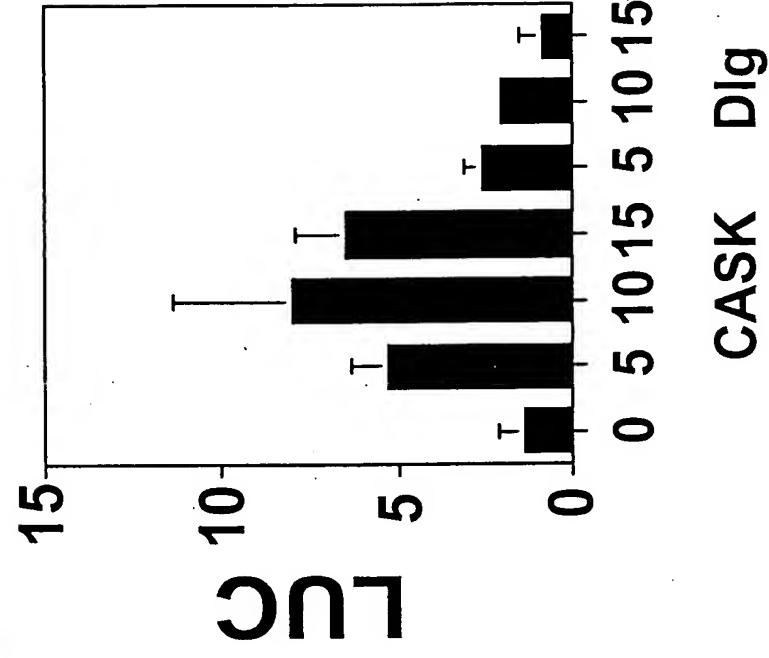
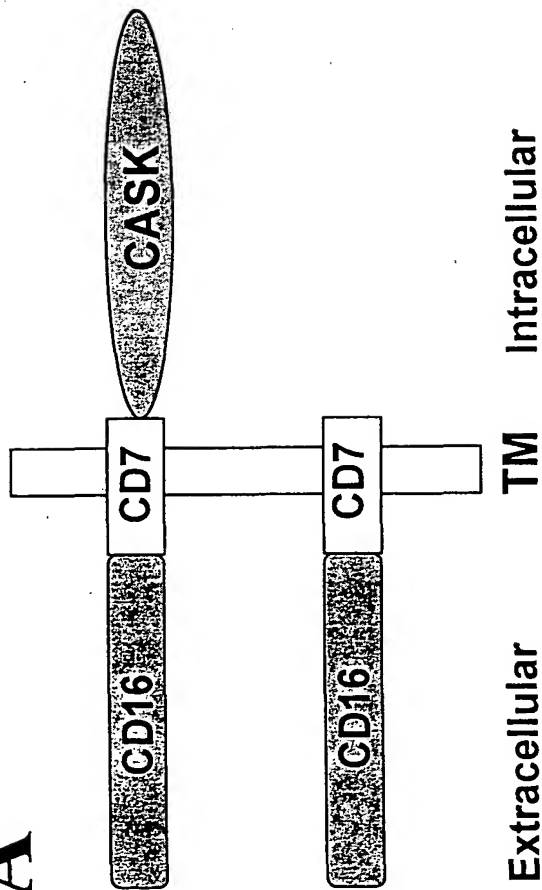


FIG. 21

A



B

16:7:CASK  $Ca^{++}$  Mobilization

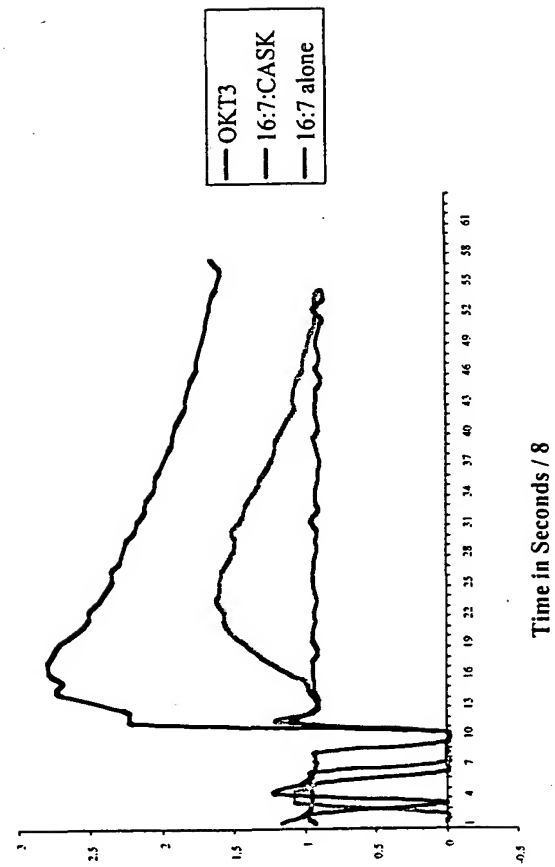


FIG. 22

# Dlg and CASK Binding Patterns

Discs Large



	<u>Zap70</u>	<u>SLP76</u>	<u>Vav</u>	<u>cdc42</u>
<u>Lck</u>	+	-	+	+
<u>LAT</u>	-	-	-	-
<u>Cbl</u>	-	-	-	-
<u>LFA-1</u>	-	-	-	-

Dlg

CASK

CASK

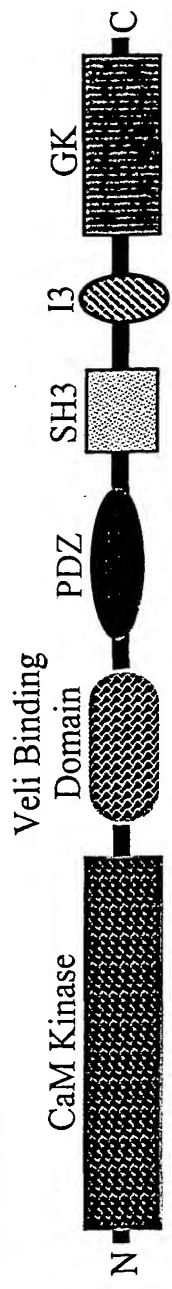


FIG. 23